

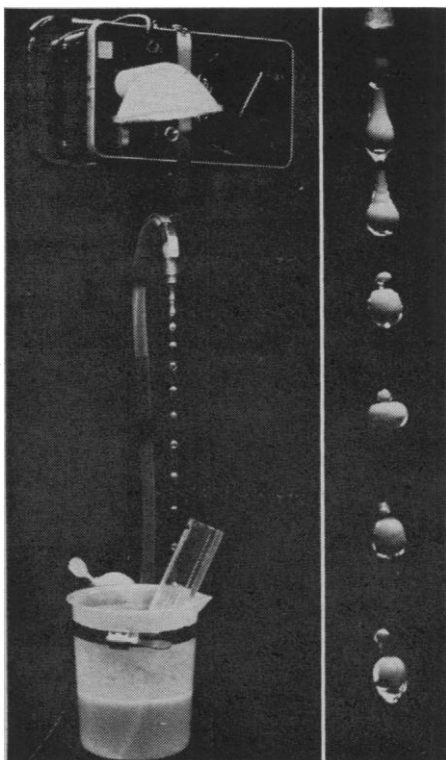


Fig. 1. (Left) Drop-display equipment. (Right) Close-up taken with a half-second exposure at  $f/16$  on plus-X film; a General Radio Company Strobotac, set at line frequency, was used for illumination.

used to give the drops a greenish glow which makes them very distinct. A variac set at 70 volts or a series resistor of about 300 ohms is used to control the output, since the pump is too vigorous when used with 115 volts and a 5-mm nozzle. The water patterns at full voltage are very interesting but exhibit some irregular motions that are not present with reduced voltage.

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### Active Transport of 5,5-Dimethyl-2,4-Oxazolidinedione

Data such as those presented by Dietschy and Carter (1), from which they conclude that 5,5-dimethyl-2,4-oxazolidinedione (DMO) is "actively transported" in the intestine, can be more plausibly interpreted in other terms. There have been other reports of weak organic acids being distributed across the intestinal wall with gradients that might be thought to suggest active

transport. Smyth and Taylor (2) found that fatty acids reach higher concentrations on the serosal than on the mucosal side of the intestine in vitro. Hogben *et al.* (3) in steady state intestinal perfusion experiments in vivo found much higher concentrations of unbound salicylic acid in plasma than in the perfusing solution, even when its pH was higher than that of plasma. They suggested that data such as these can be interpreted in terms of passive diffusion of the undissociated form of the acid without recourse to the concept of "active transport" in the usual sense. They postulated a narrow zone adjacent to the mucosal surface having a pH value lower than that of the bulk phase in which pH can be measured. Between this acidic phase and the bulk phase of higher pH adjoining it there would be no barrier to diffusion of either the ionic or undissociated species of the acid. The postulated acid zone is consistent with a number of studies, cited by Hogben *et al.*, indicating secretion of hydrogen ions by intestinal mucosa. Evidence strongly supporting the hypothesis of Hogben *et al.* is their finding that bases are concentrated in a direction opposite to that in which acids are concentrated.

As these authors pointed out, the maintenance of a concentration gradient of a partially ionized substance through this mechanism entails the expenditure of energy in the process of secretion of hydrogen ions, but this is not active transport of the organic compound in the sense in which this term is generally understood or in the sense in which Dietschy and Carter are using it.

It seems unlikely that DMO is actively transported across the intestinal mucosa or across any cellular membranes. It would be remarkable if acids of such diverse structures as fatty acids, salicylic acid, and DMO were all actively transported in the intestine in one direction and bases actively transported in the opposite direction. Rapid shifts of DMO between intracellular and extracellular water occur in response to changes in the pH of the extracellular phase. There can be no doubt that the cause of these shifts is a change in the degree of ionization of DMO, and there is no reason to believe that the movement of DMO into or out of a cell ever involves any process other than passive diffusion of the undissociated form.

Dietschy and Carter use their inter-

pretation of "active transport" of DMO to question the validity of using that substance to measure intracellular pH. Aside from the question of "active transport," if there were any situation, such as Hogben *et al.* postulate for intestine, in which cellular surfaces were surrounded by a zone of pH different from that of the bulk phase of extracellular water in which pH can be directly measured, calculation of intracellular pH from the distribution of any weak acid or base would of course not be valid. However, in the actual applications of the methods based on the distribution of carbon dioxide or of DMO, there is no reason to believe that the measurements of intracellular pH have been seriously in error because of inhomogeneity of the extracellular water with respect to pH brought about by secretion of hydrogen ions at the cellular membranes or by any other process.

Convincing evidence against the active transport of DMO in skeletal muscle is the close agreement between the intracellular pH calculated from the distribution of DMO and that calculated from the distribution of carbon dioxide. It is generally agreed that there is only a small gradient of carbon dioxide tension from the interior to the exterior of a cell, and that this gradient is determined by diffusion. Conway (4) sought to discredit the carbon dioxide method of intracellular pH measurement with the contention that a part of the acid-labile carbon dioxide in muscle is not derived from bicarbonate. Dietschy and Carter now question the validity of the DMO method on the basis of "active transport." It would indeed be an amazing coincidence if two methods, each seriously in error for an entirely different reason, should yield the same erroneous value. A more credible view is that the distribution of DMO and that of carbon dioxide both furnish valid estimates of the intracellular pH of muscle.

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